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Serum concentrations of organochlorine compounds and endometrial cancer risk (United States)

Susan R. Sturgeon, John W. Brock, Nancy Potischman, Larry L. Needham, Nathaniel Rothman, Louise A. Brinton, and Robert N. Hoover

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***Objectives*: Endogenous and exogenous estrogens are important in the development of endometrial cancer. Several organochlorine compounds, such as o,p′-DDT, have estrogenic properties. The objective of this case-control analysis was to examine serum concentrations of organochlorine compounds and risk of endometrial cancer.**

***Methods*: Analyses were based on a sample of 90 endometrial cancer cases and 90 individually matched community controls from a multicenter case-control study in five geographic regions of the United States. Information on potential confounders, including menstrual and reproductive factors, cigarette smoking, diet, and weight, was obtained by interview.**

***Results*: The adjusted relative risk of endometrial cancer in the highest quartile of exposure compared with women in the lowest quartile was 0.7 (95 percent confidence interval [CI] = 0.2-2.0) for p,p′-DDE, and 0.9 for total polychlorinated biphenyls (PCBs) (CI = 0.4-2.5).**

***Conclusions*: These findings do not support the hypothesis that organochlorine compounds are linked to the development of endometrial cancer.** *Cancer Causes and Control* **1998, 9, 417–424**

Key words: Endometrial cancer, DDT, PCB, organochlorines, United States, women.

Introduction

DDT was introduced as an organochlorine insecticide in the United States in the 1940s but was banned in 1972 due to its adverse effects on wildlife. Technical DDT typically has 77 percent p,p′-DDT (the insecticide), 15 percent o,p′-DDT, and lesser amounts of other derivatives.[1] Upon ingestion, p,p′-DDT is quickly metabolized to the highly persistent lipophilic metabolite p,p′-DDE. Dietary meat and fish are primary sources of exposure to p,p′-DDE.

Studies have shown a positive association[3,4] or no association[5-10] between past exposure to DDT and risk of breast cancer. An association is biologically plausible because several DDT isomers are weakly estrogenic. In general, o,p′-DDT is presumed to be more estrogenic than p,p′-DDT,[11] but the reverse has also been reported.[12] The primary metabolite, p,p′-DDE, has very little estrogenic potential[13] but it has been shown to be an androgen receptor antagonist.[14]

Drs Sturgeon, Potischman, Rothman, Brinton, and Hoover are with the Division of Cancer Epidemiology and Genetics, National Cancer Institute, Bethesda, MD, USA. Drs Brock and Needham are with the National Center for Environmental Health, Centers for Disease Control, Atlanta, GA, USA. Address correspondence to Dr Sturgeon, Hormonal Studies Section, Environmental Epidemiology Branch, National Cancer Institute, Executive Plaza North, Room 443, Bethesda, MD 20852, USA.

Polychlorinated biphenyls (PCBs) are a series of 209 congeners of chlorinated aromatic hydrocarbons. PCBs were introduced in the 1920s and were widely used in capacitors and transformers. Owing to concern over the persistence of PCBs in the environment, production ceased during the 1970s in the US.[15] Certain PCBs have weak estrogenic properties[16-17] and others can induce cytochrome P450 enzymes, thus potentially affecting steroid metabolism.[18] Some studies have suggested a possible link between PCBs and breast cancer [2,3,10] but others have not observed an association.[7-8]

The effects of menopausal estrogens on breast cancer are considerably weaker than the five- to 10-fold increased risks found between estrogen use and endometrial cancer.[19] Thus, one might reasonably expect that estrogenic effects of organochlorine compounds would be easier to detect on endometrial than on breast tissue.[20] We studied the relation between serum levels of DDT-related compounds and PCBs using a sample of endometrial cancer cases and their matched controls from a large multicenter case-control study. Data on other organochlorine pesticides were also available from the same laboratory procedure.

Materials and methods

This study was conducted in collaboration with seven hospitals in five geographic areas of the US: Chicago, Illinois; Hershey, Pennsylvania; Irvine and Long Beach, California; Minneapolis, Minnesota; and Winston-Salem, North Carolina.[21] Cases were newly diagnosed with endometrial cancer between 1 June 1987 and 15 May 1990; were aged 20 to 74 years; and lived in defined geographic areas. Controls under age 65 years were selected using random-digit-dialing techniques (RDD) whereas older controls were selected with information provided by the Health Care Financing Administration. Control subjects were individually matched to case patients by age (same five-year age group), race (White, Black, or other), and area of residence (telephone exchange or zip code). A short telephone questionnaire was administered to all potential control subjects to determine hysterectomy status. Control subjects without an intact uterus were replaced with another eligible subject.

A structured interview, on average 60 min in length, was administered to obtain information on hypothesized risk factors, including demographics, pregnancy history, menstrual history, contraceptive behavior, use of exogenous hormones, diet and alcohol intake, and physical activity. A variety of anthropometric measurements were also obtained, including waist and thigh circumference to estimate body fat distribution. Cases were interviewed in the hospital and controls were interviewed in their homes.

Interviews were completed with 434 of 498 eligible cases (87.1 percent) and with 313 of 477 eligible controls (65.6 percent). The primary reason for nonresponse was refusal (4.8 percent of cases *cf* 21.8 percent of controls). All cases were pathologically confirmed with 93 percent of the interviewed cases having a classification of epithelial cancer. Because of the distinct epidemiologic characteristics of sarcomas,[22] 29 cases with sarcomas and 16 matched controls were removed from the analysis.

Blood collection

Participants were asked to provide a fasting blood sample. Nurse interviewers collected samples from cases prior to surgery. A phlebotomist visited controls in their homes usually one month after the home interview. Each field center processed and stored serum samples at -70° C until the specimens were shipped on dry ice to a central storage facility where they were kept at −85° C. Of the interviewed subjects, 325 cases and 217 control subjects donated blood.

Organochlorine analysis

A total of 90 sets of interviewed cases and individually matched control subjects had sufficient blood volume required for organochlorine analyses remaining in storage. Serum samples were arranged in a set consisting of a case and a matched control. Blinded samples were analyzed at the National Center for Environmental Health, Centers for Disease Control and Prevention. A reagent blank (to check for contaminants) and an internal laboratory quality-control sample (spiked bovine serum)[23] were analyzed with every 10 study serum samples. Each sample was extracted using solid phase extraction and then analyzed on two separate gas chromotographs with electron-capture detection. The chromatographs used different columns (DB5 and DB1701) to reduce interferences and improve selectivity. Results were obtained for: four DDT-related compounds (o,p′-DDT, p,p′-DDT, o,p′-DDE, p,p-DDE); 27 PCB congeners (BZ# 28, 52, 56, 66, 74, 99, 101, 105, 110, 118, 138, 146, 153, 156, 170, 172, 178, 180, 183, 187, 189, 193, 194, 195, 201, 203, and 206); and 13 other organochlorine compounds using methods as previously described.[23]

Serum samples were analyzed for total cholesterol and triglycerides, and total lipids were calculated by a standard formula to correct for possible differences in recent food intake.[24] Lipid-corrected individual organochlorine concentrations were calculated by dividing by total lipids.

Summary lipid-corrected concentrations of total PCBs were calculated by dividing each PCB congener

by total lipids and adding them together. The congeners measured in this study were also assigned into three groupings based on a classification scheme proposed by Wolff and colleagues:[17] (i) potentially estrogenic (BZ# 52, 101, 187, 177, 201); (ii) potentially anti-estrogenic (BZ# 66, 74, 105, 118, 156, 138); and (iii) cytochrome P450 enzyme inducers (99, 153, 203, 183). Because BZ# 138 is a highly prevalent, di-ortho congener with limited anti-estrogenic activity,[17] a potentially anti-estrogenic summary variable restricted to mono-ortho congeners was also created (BZ# 66, 174, 105, 118, 156).

Samples from 22 study subjects were selected at random and tested in duplicate. Duplicate testing was performed in a blind fashion. The coefficients of variation, calculated as the standard deviation of the level divided by the mean level, were 9.9 percent for p,p'-DDE and 18.5 percent for total PCBs. Coefficients of variation for other organochlorine compounds were considerably higher but concentrations of these compounds were frequently below the formal limits of detection of the assays.

Formal detection limits for the various assays range from 0.54 to 0.66 ng/ml for the DDT-related compounds, 0.17 to 0.45 ng/ml for the PCB congeners, and 0.08 to 0.42 ng/ml for the other organochlorine pesticides.[23] These detection limits were designed to eliminate 99.86 percent of false-positive results. Because such conservative detection limits can result in a loss of valid data, concentrations obtained below these formal method detection limits were not eliminated in the present analysis.

Statistical analysis

Summary data for the cases and the controls in each set are described by the median value and 25th and 75th percentiles cut-points. Case-control differences were tested by the Wilcoxon signed rank test. Conditional logistic regression was used to derive relative risk estimates (RR) and 95 percent confidence intervals (CI). Cut-points for categorical exposure variables were usually based upon their quartile distribution among controls. When more than 25 percent of the controls had no measurable concentration of the exposure of interest, however, cut-points were determined by grouping controls with no measurable levels and dividing remaining controls into two equal groups.

Because organochlorine compounds are stored in adipose tissue, risk estimates are presented with and without adjustment for body weight. None of the following individual factors materially changed the results presented and were not included as confounders in logistic models: menopausal estrogen use, age at menarche, waist-to-thigh circumference ratio, saturated fat intake, total calories, oral contraceptive use, smoking status, and parity.

Results

The mean ages of the cases and controls were 57.2 and 57.9 years, respectively. Over 90 percent of the women were White, non-Hispanics. Previously identified risk factors for endometrial cancer[21,25-29] among women with organochlorine data are presented in Table 1. Compared with control subjects, cases were more likely to be nulliparous, to use menopausal estrogens, to be obese, to

Table 1. Relative risks (RR) and 95 percent confidence intervals (CI) for endometrial cancer associated with selected characteristics; US areas

Characteristic	Cases	Controls	RR (CI)
Number of livebirths			
0	24	10	1.0 —
1-2	33	35	0.3 (0.1-0.9)
3+	33	45	0.2 (0.1-0.6)
Menopausal estrogens			
Never	71	74	1.0 —
Ever	18	15	1.3 (0.6-3.0)
< 10 yrs	9	12	0.8 (0.3-2.2)
10+ yrs	9	3	2.9 (0.8-10.9)
Weight (lbs)[a]			
< 125	12	24	1.0 —
125-149	22	27	1.2 (0.4-3.7)
150-174	14	23	0.8 (0.3-2.2)
175+	41	16	3.7 (1.4-9.8)
Waist-to-thigh circumference ratio[b]			
< 1.62	14	26	1.0 —
1.62-1.78	13	26	0.6 (0.2-2.0)
1.79-1.99	30	18	3.1 (1.1-8.9)
> 1.99	30	18	2.7 (0.9-8.7)
Age at menarche (yrs)			
14+	22	33	1.0 —
13	21	24	1.4 (0.5-3.4)
≤ 12	46	33	1.9 (1.0-3.8)
Saturated fat (g/day)			
< 12	16	18	1.0 —
13-18	21	23	1.0 (0.4-2.5)
19-25	23	29	0.9 (0.4-2.5)
> 25	28	20	1.6 (0.6-4.3)
Oral contraceptives			
Never	69	57	1.0 —
Ever	21	33	0.5 (0.2-1.0)
Cigarette use			
Never	59	51	1.0 —
Former	24	24	0.8 (0.4-1.8)
Current	6	15	0.3 (0.1-0.9)
Calories (kcals)[b]			
Q1 (< 975)	17	22	1.0 —
Q2 (975-1,247)	16	20	1.3 (0.5-3.3)
Q3 (1,248-1,560)	28	28	1.3 (0.5-3.6)
Q4 (> 1,560)	27	20	2.3 (0.8-6.6)

[a] Adjusted for waist-to-thigh circumference ratio.
[b] Adjusted for weight.

have a high waist-to-thigh circumference ratio, to have an earlier age at menarche, to have high saturated fat intakes, and to consume more calories. However, they were less likely to use oral contraceptives, and to be current smokers. Unlike in other investigations, late age at natural menopause was not found to be associated with endometrial cancer in the present analysis or in the original case-control study.[21]

There was no significant difference in the lipid-corrected serum concentration of p,p′-DDE between cases and controls (Table 2). By contrast, p,p′-DDT concentrations were significantly higher in cases than controls. In addition, o,p′-DDT concentrations were higher in controls than cases, although this difference was not statistically significant. There were no significant differences in the concentrations of total PCBs, estrogenic PCBs, or anti-estrogenic PCBs between cases and controls. Concentrations of enzyme-inducing PCBs were slightly higher in controls than cases but this comparison was only marginally significant. Eight organochlorine compounds (o,p′-DDE, aldrin, endrin, alpha-chlordane, gamma-chlordane, gamma-hexachlorocyclohexane, heptachlor, and mirex) were detected in fewer than 15 percent of the cases and controls and were excluded from all analyses. Of the six other compounds, only dieldrin concentrations were significantly higher in cases than controls.

We found no evidence of a positive association between high serum concentrations of p,p′-DDE and risk of endometrial cancer (Table 3). Compared with women in the lowest tertile of p,p′-DDT, women in the highest tertile were at nonsignificantly higher risk of endometrial cancer (multivariate RR = 1.8, CI = 0.7-4.4). Compared with women in the lowest tertile of o,p′-DDT, women in the highest tertile were at somewhat decreased risk (multivariate RR = 0.5, CI = 0.1-1.9).

There were no positive associations between endometrial cancer risk and high serum concentrations of total PCBS, estrogenic PCBs, or enzyme-inducing PCBs (Table 4). Although women in the second, third, and fourth quartiles of enzyme-inducing PCBs were at decreased risk compared with women in the lowest quartile, there was no gradient of decreasing risk with increasing concentration. Compared with women in the lowest quartile of anti-estrogenic PCBs, the multivariate RR for women in the highest quartile was 1.1 (CI = 0.4-3.1). RRs associated with anti-estrogenic PCBs except BZ# 138 by quartile were: 1.0, 3.2 (CI = 1.1-9.2), 1.5 (CI = 0.5-4.2), and 2.6 (CI = 0.8-8.2).

Dieldrin-associated multivariate RRs for endometrial cancer by tertile were: 1.0; 2.1 (CI = 0.9-4.2); and 1.9 (CI = 0.7-4.8). No increases in risk were observed for the other five organochlorine compounds (Table 5).

Because risk factors for endometrial cancer may vary according to menopausal status, additional analyses were restricted to the 72 matched sets of women who were 50 years or older. Results were similar to those presented for the overall group. Results were also similar when analyses were restricted to the 65 subjects with early-stage endometrial cancer and their matched controls.

Because serum concentrations of many organochlorine compounds were low, statistical analyses were repeated using only two exposure categories (below; and at the level of detection of the analyte and above). For summary exposure variables, the sum of the limit of detection values for the relevant compounds was used

Table 2. Distribution of lipid-corrected organochlorine serum concentrations in endometrial cancer cases and matched controls; US areas

	Cases Median (25th, 75th)	Controls Median (25th, 75th)	P^a
DDT-related compounds			
p,p′-DDE	1,417 (809,2169)	1,358 (943,2276)	0.58
o,p′-DDT	11 (0,68)	19 (0,83)	0.09
p,p′-DDT	69 (0,126)	0 (0,96)	0.03
Summary PCB indices			
Total PCBs	302 (205,510)	350 (237,595)	0.48
Estrogenic PCB	1 (0,5)	1 (0,5)	0.84
Antiestrogenic PCB	166 (111,286)	176 (111,301)	0.86
Enzyme-inducing PCB	81 (47,141)	102 (67,178)	0.08
Other organochlorines			
Beta-hexachlorocyclohexane	38 (10,86)	35 (10,71)	0.37
Dieldrin	8 (0,29)	0 (0,15)	0.03
Hexachlorobenzene	43 (31,62)	45 (35,63)	0.32
Heptachlor epoxide	0 (0,16)	0 (0,4)	0.08
Oxychlordane	0 (0,23)	1 (0,22)	0.56
Trans-nonachlor	2 (0,45)	10 (0,45)	0.54

[a] Wilcoxon signed-rank test.

Table 3. Relative risks (RR) and 95 percent confidence intervals (CI) for endometrial cancer associated with lipid-corrected DDT-related compounds; US areas

	Organochlorine concentration			Cases	Controls	RR[b]	RR[b,c] (CI)
	Range (ng/g lipid)	Mean (ng/g lipid)	Mean (ng/mL)				
p,p′-DDE							
1	256-943	679	3.9	27	23	1.0	1.0 —
2	954-1,357	1,172	6.0	17	22	0.7	0.5 (0.2-1.2)
3	1,359-2,276	1,833	9.1	27	23	1.0	1.0 (0.4-2.5)
4	2,391-10,486	4,102	19.9	19	22	0.7	0.7 (0.2-2.0)
o,p′-DDT[a]							
1	0	0	0	43	39	1.0	1.0 —
2	5-75.8	36.6	0.2	27	26	0.8	0.9 (0.4-2.1)
3	78.2-386.6	129.8	0.6	20	25	0.5	0.5 (0.1-1.9)
p,p′-DDT[a]							
1	0	0	0	41	50	1.0	1.0 —
2	31.6-98.2	76.1	0.4	15	20	0.9	0.6 (0.2-1.6)
3	99.0-278	155.0	0.7	34	20	2.3	1.8 (0.7-4.4)

[a] Cut-points were determined by grouping controls with no measurable levels and dividing remaining controls into two equal groups.
[b] Adjusted for matching factors.
[c] Additionally adjusted for weight.

for the cut-point. Results were comparable to those presented with two exceptions: the RRs associated with serum levels above the level of detection were 0.8 (CI = 0.3-2.2) for dieldrin and 2.3 (CI = 0.8-7.0) for oxychlordane. This analytic approach was not relevant for p,p′-DDE (all subjects above the level of detection), total PCBs, and estrogenic PCBs (more than 97 percent of subjects below the level of detection).

Limited data are available on the recoveries of the various pesticides and PCB congeners from the laboratory method employed in this study. In a small published study,[23] recoveries varied from 47.0 percent

Table 4. Relative risks (RR) and 95 percent confidence intervals (CI) for endometrial cancer associated with lipid-corrected PCB-related compounds

	Organochlorine concentration			Cases	Controls	RR[b]	RR[b,c] (CI)
	Range (ng/g lipid)	Mean (ng/g lipid)	Mean (ng/mL)				
Total PCB							
1	(28-237)	165	0.9	30	23	1.0	1.0 —
2	(241-349)	284	1.5	24	22	0.8	1.1 (0.4-3.0)
3	(362-595)	462	2.2	17	23	0.6	0.7 (0.3-2.0)
4	(598-1,714)	816	4.1	19	22	0.7	0.9 (0.4-2.5)
Estrogenic PCBs[a]							
1	(0)	0	0	34	30	1.0	1.0 —
2	(0.1-3.3)	1.1	0.01	27	31	0.8	1.1 (0.5-2.4)
3	(3.4-90)	16	0.09	29	29	0.9	1.3 (0.5-3.2)
Anti-estrogenic PCBs							
1	(4-111)	75	0.4	23	23	1.0	1.0 —
2	(112-174)	138	0.8	23	22	1.0	1.2 (0.5-3.2)
3	(180-301)	229	1.1	25	23	1.1	1.2 (0.4-3.0)
4	(309-1,254)	454	2.3	19	22	0.9	1.1 (0.4-3.1)
Enzyme-inducing PCBs							
1	(0-67)	36	0.2	35	23	1.0	1.0 —
2	(70-101)	85	0.4	19	22	0.5	0.6 (0.2-1.5)
3	(103-178)	136	0.7	20	23	0.5	0.7 (0.3-1.8)
4	(183-442)	247	1.2	16	22	0.4	0.6 (0.2-1.6)

[a] Cut-points were determined by grouping controls with no measurable levels and dividing remaining controls into two equal groups.
[b] Adjusted for matching factors.
[c] Additionally adjusted for weight.

Table 5. Relative risks (RR) and 95 percent confidence intervals (CI) for endometrial cancer associated with lipid-corrected organochlorine pesticides; US areas

	Organochlorine concentration			Cases	Controls	RR[b]	RR[b,c] (CI)
	Range (ng/g lipid)	Mean (ng/g lipid)	Mean (ng/mL)				
Beta-hexachlorobenzene							
1	(0-9.6)	2.3	0.01	22	23	1.0	1.0 —
2	(9.9-35.2)	21.1	0.12	20	22	0.9	0.8 (0.3-2.3)
3	(35.3-70.8)	51.4	0.26	18	23	0.8	0.5 (0.1-1.4)
4	(73.9-938)	144.3	0.78	30	22	1.5	0.9 (0.3-2.6)
Dieldrin[a]							
1	(0)	0	0	32	51	1.0	1.0 —
2	(0.4-20.5)	9.2	0.05	28	20	2.2	2.1 (0.9-4.2)
3	(21.5-189.1)	61.0	0.31	30	19	2.9	1.9 (0.7-4.8)
Hexachlorobenzene							
1	(0-34.8)	21.7	0.13	27	23	1.0	1.0 —
2	(35.0-44.9)	40.3	0.20	21	22	0.7	0.6 (0.2-1.8)
3	(45.3-63.3)	54.5	0.28	20	23	0.7	0.5 (0.2-1.7)
4	(63.5-574.7)	102.3	0.45	22	22	0.7	0.8 (0.2-2.6)
Oxychlordane[a]							
1	(0)	0	0	47	44	1.0	1.0 —
2	(0.2-20.3)	9.5	0.05	19	23	0.8	0.6 (0.3-4.6)
3	(22.3-145.5)	51.9	0.26	24	23	1.0	1.2 (0.5-3.0)
Trans-nonachlor[a]							
1	(0)	0	0	40	35	1.0	1.0 —
2	(0.4-38.1)	15.8	0.08	24	28	0.7	0.6 (0.2-1.5)
3	(38.6-310.6)	92.7	0.48	26	27	0.8	0.7 (0.3-1.9)
Heptachlor epoxide[a]							
1	(0)	0	0	56	60	1.0	1.0 —
2	(0.4-23.1)	7	0.04	12	15	0.9	0.6 (0.2-2.0)
3	(24.1-205.6)	66.1	0.36	22	15	1.6	1.0 (0.4-2.7)

[a] Cut-points were determined by grouping controls with no measurable levels and dividing remaining controls into two equal groups.
[b] Adjusted for matching factors.
[c] Additionally adjusted for weight.

to 70.1 percent for the DDT-related compounds, from 42.3 percent to 76.8 percent for the PCB congeners, and from 51.5 percent to 80.9 percent for the other pesticides. Results for variables involving only one organochlorine compound (*e.g.*, p,p-DDE) would not be affected by recovery adjustments because the correction method involves dividing by a constant. When recoveries of the relevant PCB congeners were considered in the calculation of summed PCB variables (*e.g.*, total PCBs), relative risk estimates for these variables were essentially unchanged (data not shown).

Discussion

A link between exposure to DDT and other organchlorine compounds and the risk of breast cancer is biologically plausible because some organochlorine compounds are weakly estrogenic.[12,11,15,16] A few early studies were positive[11-13,15-16] but several recent larger investigations have been null.[5-8] Use of menopausal estrogens and high endogenous levels of unopposed estrogens are associated with markedly increased risks of endometrial cancer.[19,30] It is generally accepted that endometrial cancer is a more estrogen-related tumor than breast cancer. Adami and colleagues[20] recently suggested that the focus of organochlorine research should shift from breast to endometrial cancer because the latter is more likely to be a bellwether of weak estrogenic effects.

This study, the first we know of to examine the relation between serum organochlorine concentrations and risk of endometrial cancer, did not find an association between serum concentrations of p,p-DDE, the major metabolite of DDT, and endometrial cancer. Risk was slightly increased among women with higher serum concentrations of p,p'-DDT. This finding is of some interest in view of a recent evidence that p,p'-DDT is effective in regulating estrogen receptor-mediated cellular responses.[12] However, the interpretation of this result is complicated by the fact that the concentration of another presumably estrogenic derivative, o,p'-DDT,[11] was lower in cases than controls.

In the present study, no associations were observed between elevated serum concentrations of several PCB-related indices, including total PCBs and potentially estrogenic PCBs, and endometrial cancer risk. Higher concentrations of potentially enzyme-inducing PCBs were associated with somewhat lower risk of endometrial cancer but the absence of a dose-response pattern tends to argue against a causal association.

Although only a small proportion of the subjects from the original study had serum analyzed, RR estimates from the present study for recognized risk factors were similar to those for the total group and from other studies.[21,25-29] In addition, selected characteristics were approximately as prevalent in our case group as in the nearly 500 women from the original case group, including menopausal estrogen use (20 *cf* 19 percent), oral contraceptive use (23 *cf* 20 percent), weight of 175 pounds or more (45 *cf* 43 percent), and cigarette smoking (33 *cf* 32 percent). These similarities suggest that the current results are unbiased and probably generalizable to endometrial cancer in the total population.

In the present study, median recovery-adjusted and -unadjusted serum concentrations among controls for p,p′-DDE were 9.8 ng/ml and 7.0 ng/ml, respectively. Comparable concentrations of total PCBs were 2.4 ng/ml and 1.6 ng/ml. The concentration of p,p′-DDE we observed is similar to levels reported from two other studies that obtained serum between 1985 and 1991[2,7] but it is approximately six times lower than level reported from the San Francisco Bay area during the late 1960s.[5] The concentration of PCBs is approximately half the levels obtained from these other studies.[2,5,7] Conceivably, higher concentrations of organochlorine compounds such as those present when DDT was still being used may be related to endometrial cancer. Finally, a large number of organochlorine compounds were investigated in this study and it is possible that the small associations observed for p,p-DDT and dieldrin may have occurred by chance.

The debate on the role of organochlorines and hormone-related cancers will likely be resolved as results are obtained from ongoing studies. The present study does not lend support to the hypothesis that organochlorine compounds are important in the development of endometrial cancer.

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